

10/567411

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
29 December 2004 (29.12.2004)

PCT

(10) International Publication Number  
**WO 2004/112835 A2**

- (51) International Patent Classification<sup>7</sup>: **A61K 39/395** Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU (GB).
- (21) International Application Number:  
PCT/GB2004/002647 (74) Agent: MARCHANT, James; Elkington and Fife, 8 Pembroke Road, Sevenoaks, Kent TN13 1XR (GB).
- (22) International Filing Date: 18 June 2004 (18.06.2004) (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0314461.5 20 June 2003 (20.06.2003) GB
- (71) Applicant (for all designated States except US): **ISIS INNOVATION LTD** [GB/GB]; Ewert House, Ewert Place, Summertown, Oxford OX2 7SG (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **BUSHELL, Andrew** [GB/GB]; Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU (GB). **WOOD, Kathryn** [GB/GB]; Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU (GB). **KARIM, Mahzuz** [GB/GB]; Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU (GB). **OLIVEIRA, Vanessa** [PT/GB]; Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU (GB). **SAWITZKI, Brigit** [DE/GB];
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/112835 A2

(54) Title: SUPPRESSION OF TRANSPLANT REJECTION

(57) Abstract: Transplant rejection in an animal is suppressed by administration of an antibody directed at a cell surface antigen selected from the group consisting of CD4, CD8, CD154, LFA-1, CD80, CD86 and ICAM-1, preferably an anti-CD4 antibody, together with a non-cellular protein antigen to generate in the animal a population of regulatory T-lymphocytes; reactivating said population of regulatory T-lymphocytes by further administration to the animal of the non-cellular protein antigen; and transplanting said organ or tissue whilst said population of regulatory T-lymphocytes is activated. Regulatory T cells can be generated ex vivo by culturing T cells with an antibody directed at a cell surface antigen selected from the group consisting of CD4, CD8, CD154, LFA-1, CD80, CD86 and ICAM-1, in the presence of cells that present either alloantigen or a non-cellular protein antigen. Ex vivo generated T-lymphocytes can be used as an alternative method of overcoming transplant rejection or in combination with the in vivo method. A similar approach can be adopted for the treatment of autoimmune conditions.